

Attachment

Basi, Nirmal

To: IFW Image Problem
Subject: Problem Image - ASN: 09688286

Application Serial Number (ASN): 09688286

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Document Type: SPEC

Number of Pages: 3

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Received a printer rush because some of the pages are illegible or incompletely scanned. Please rescan the following pages:

- 1) Specification (original 10/13/200), subscripts on page 13, lines 1 and 2 are not legible.
- 2) Specification dated 02/04/2003, amended paragraph on page 37, line 3 is incomplete.
- 3) Amended claim 43 on Examiners Amendment dated 04/08/2003 is illegible and incomplete. The cover page of the same Amendment (Notice of Allowability) is folded when scanned and not legible.
- 4) The 1449 dated 04/08/03, last entry on pages 2 and 3 are illegible and incomplete
- 5) Sequence listing dated 03/22/2004 is not legible

Examiner Nirmal Basi

Art Unit 1646

tel 571-272-0868

- 13 -

In addition, peptides can be conformationally constrained by, for example, incorporation of C_α and N_ε-methylamino acids, introduction of double bonds between C_α and C_β atoms of amino acids and the formation of cyclic peptides or analogues by introducing covalent bonds such as forming an amide bond between the N and C termini, between two side chains or between a side chain and the N or C terminus.

These types of modifications may be important to stabilise NR4 if administered to an individual or for use as a diagnostic reagent

- 10 The present invention further contemplates chemical analogues of NR4 capable of acting as antagonists or agonists of NR4 or which can act as functional analogues of NR4. Chemical analogues may not necessarily be derived from NR4 but may share certain conformational similarities. Alternatively, chemical analogues may be specifically designed to mimic certain physiochemical properties of NR4. Chemical analogues may be chemically synthesised or may
15 be detected following, for example, natural product screening.

The identification of NR4 permits the generation of a range of therapeutic molecules capable of modulating expression of NR4 or modulating the activity of NR4. Modulators contemplated by the present invention includes agonists and antagonists of NR4 gene expression or NR4
20 protein activity. Antagonists of NR4 gene expression include antisense molecules, ribozymes and co-suppression molecules. Agonists include molecules which increase promoter ability or interfere with negative regulatory mechanisms. Agonists of NR4 protein include antibodies, ligands and mimetics. Antagonists of NR4 include antibodies and inhibitor peptide fragments. Where a cell co-expresses NR4 and IL-4 receptor α -chain, agonists and antagonists may target
25 the IL-4 receptor α -chain.

identical between the predicted murine and human proteins are indicated by (*). DNA encoding the murine signal sequence is underlined, with A26 or T27 being the predicted first amino acid of the mature protein.--

Please amend the paragraph beginning at page 33, line 12, as follows:

--Figure 10 is a representation of the N-terminal amino acid sequence of murine NR4 (SEQ ID NOS: 10 and 11).--

Please amend the paragraph beginning at page 37, line 3, as follows:

--A library was constructed λZAP II using Apol digested genomic DNA from embryonal stem cells and screened with a pool of ³²P-labelled oligonucleotides encoding the amino acid sequence Trp-Ser-Asp-Trp-Ser (SEQ ID NO: 12) found in many members of the haemopoietin receptor family. One hybridising bacteriophage clone was found to contain a sequence that appeared to encode part of a novel member of the haemopoietin receptor family. This receptor was given the operational name NR4. The sequence of the genomic clone was used to isolate cDNAs encoding NR4 from WEHI-3B cell, peritoneal macrophage, bone marrow, skin and kidney libraries. A composite of the nucleotide sequence (SEQ ID NO: 1) and predicted amino acid sequence (SEQ ID NO: 2) of these cDNAs is shown in Figure 1. The NR4 cDNA is predicted to encode for a protein of 424 amino acid residues, containing a putative signal sequence and transmembrane domain. The extracellular region of the protein contained an immunoglobulin-like domain (amino acids 27-117), in addition to a typical haemopoietin receptor domain (amino acids 118-340) which includes four conserved cysteine residues and the characteristic Trp-Ser-Asp-Trp-Ser motif (Figure: in bold as WSXWS). The cytoplasmic-tail of

incomplete

Serial Number: 09/688,286

Art Unit: 1646

17E
N 18
4/1/03
Page 2 (E, 2nd
by DMT)

DETAILED ACTION

1. Amendments filed 2/4/03 (paper number 13), 3/24/03 (paper number 15) and 3/28/03 (paper number 16) have been entered in part.

2. The rejections of record are withdrawn in view of Applicants arguments and Amendments
5 filed in paper numbers 13, 14 and 16.

3. The proposed drawing correction and/or the proposed substitute sheets of drawings, filed on 3/24/03 (paper number 15) have been approved. The application having been allowed, formal drawings are required in response to this Office Action.

Examiner's Amendment

10 4. An examiner's amendment to the record appears below. Should the changes and/or additions be unacceptable to applicant, an amendment may be filed as provided by 37 CFR 1.312. To ensure consideration of such an amendment, it MUST be submitted no later than the payment of the issue fee.

15 Authorization for this examiner's amendment was given in a telephone interview with Peter Bernstein on 3/28/03.

In the Claims:

1. Amend claims 43-48 as follows:

claim 36 or 37 and at least one of a pharmaceutically acceptable carrier or a diluent.

claim 43
← missing
data/illegible